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PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Gary Ruvkun et al.	Art Unit:	1632
Serial No.:	08/908,453	Examiner:	Ram R. Shukla
Filed:	August 7, 1997	Customer No.:	21559
Title:	AGE-1 POLYPEPTIDES AND RELATED MOLECULES AND METHODS		

BOX APPEAL
Commissioner for Patents
Washington, DC 20231

APPELLANTS' AMENDED BRIEF ON APPEAL

SUBMITTED PURSUANT TO 37 CFR § 1.192

In support of Appellants' notice of appeal filed August 5, 2002 of the Examiner's final rejection mailed on March 26, 2002, and submitted herewith in triplicate is Appellants' amended brief on appeal.

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Real Party in Interest

The Real Party in Interest is The General Hospital Corporation, to which all interest in the present application has been assigned by virtue of an Assignment, recorded on July 23, 1998 (Reel/Frame 334/0514).

Related Appeals and Interferences

There are no currently pending appeals or interferences related to this case.

Status of Claims

Claims 8, 10-13, 15, 16, 19, and 20 are currently pending. Claims 1-7, 14, and 21-28 were withdrawn from consideration. Claims 9, 17, 18, 29, and 30 were cancelled. Claims 8, 10-13, and 16 were allowed.

Claims 15, 19, and 20 were finally rejected in a Final Office Action mailed on March 26, 2002, and are appealed.

Status of Amendments

The amendment filed on June 26, 2002, has been entered, and this appeal is based on the claims pending after entry of that amendment.

Summary of the Invention

Appellants' invention generally features a purified and isolated DNA encoding an AGE-1 polypeptide having PI-3 kinase activity, and methods of identifying compounds that decrease AGE-I expression or biological activity. The claims on appeal are specifically directed to these screening methods, which require (a) a nematode cell expressing its endogenous AGE-1 DNA; (b) contacting the nematode cell with a candidate compound; and (c) measuring AGE-1 gene expression in the nematode cell, a decrease in AGE-1 gene expression following contact with the candidate compound, compared to AGE-1 gene expression in a nematode cell that is not contacted with the

candidate compound, identifying the candidate compound as a compound that is capable of decreasing AGE-1 gene expression.

Methods for screening candidate compounds are provided in Appellants' specification at page 31, line 7 to page 34, line 7. In particular, at page 31, lines 15-17, Appellants teach methods for measuring AGE-1 expression. The nucleic acid sequence of an AGE-1 cDNA is found at Figure 4 (SEQ ID NO:2). At page 31, lines 9-14, Appellants teach that AGE-1 expression may be measured following the addition of antagonist molecules either to culture medium or to an animal, for example, a nematode. At page 31, lines 17-19, Appellants teach that the level of AGE-1 expression in the presence of a candidate molecule is compared to the level measured for the same cells in the absence of the candidate molecule. In addition, Appellants teach methods for identifying compounds that modulate AGE-1 kinase activity *in vitro* at page 32, lines 8-21. Methods for the selection of candidate compounds are provided at page 31, lines 19-21. Methods for purifying such compounds are provided at page 32, lines 1-7. Appellants teach that the usefulness of compounds that modulate AGE-1 expression can be confirmed by testing the compounds in animal models such as nematodes (page 33, lines 4 and 5). Finally, at page 33, lines 6-9, Appellants teach that selected compounds may be used as therapeutics to decrease the level of native AGE-1 expression and thereby increase the longevity of an animal, for example, a human.

Issue

The issue on appeal is whether the Office erred in rejecting claims 15, 19, and 20 as lacking enablement.

Grouping of Claims

Claims 15, 19, and 20 stand or fall together.

Argument

Claims 15, 19, and 20 stand rejected, under 35 U.S.C. § 112, first paragraph, as lacking enablement. This rejection is based on the Office's assertion that in the absence of an AGE-1 promoter the skilled artisan could not know whether a compound that alters AGE-1 expression worked via a direct effect on AGE-1, or whether it worked by having an effect on another gene. The basis for the rejection is applied in error, and the rejection should be reversed.

With respect to the 35 U.S.C. § 112, first paragraph rejection, Appellant's point out that understanding how a compound alters AGE-1 expression is not relevant to enablement. As is clear from the case law:

> An inventor need not comprehend the scientific principles behind the invention. The *inventor's theory or belief as to how his invention works is not a necessary element to satisfy the enablement requirement.* (Emphasis added.) *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985)

Thus, it is irrelevant to patentability whether the compound's effect on AGE-1 expression is direct, or indirect. Appellant's claims are directed to a method for identifying a compound that alters AGE-1 expression, and this claim is clearly enabled. Indeed, the Office itself has acknowledged so much in the Advisory Action at page 2, paragraph 1, where it states:

> It is reiterated that while the cDNA of AGE-1 is taught in the specification and *an artisan would be able to see change in mRNA levels by northern analysis, in the absence of the promoter of the AGE-1*...(Emphasis added.)

This conclusion by the Office is consistent with the fact that Appellants have indeed provided a teaching in the present specification that enables the skilled artisan to practice the methods of the invention. With Appellants' invention in hand, the skilled artisan could easily screen for compounds that alter AGE-1 expression. This screening requires only two elements (i) the detection of a change in AGE-1 expression relative to the appropriate controls; and (ii) the selection of useful compounds. Appellants' specification provides methods that satisfy both of these requirements.

With respect to detecting a change in the transcription of AGE-1, Appellants disclose, at page 31, lines 15-17, that AGE-1 expression may be measured, for example, by standard Northern blot analysis using an AGE-1 nucleic acid, or fragment thereof, as a hybridization probe. Appellants teach the nucleic acid sequence of an AGE-1 cDNA at Figure 4 (SEQ ID NO:2), and Appellants disclose, at page 31, lines 15 and 16, that Ausubel et al. (*Current Protocols in Molecular Biology*, 1996, Wiley & Sons, New York, NY) provide methods for carrying out a Northern blot. Nothing more is required to measure a change in AGE-1 gene expression.

With respect to teaching the appropriate controls, Appellants' specification, at page 31, lines 9-14, specifically teaches that AGE-1 expression may be measured following the addition of antagonist molecules either to culture medium or to an animal, for example, a nematode. Appellants further disclose, at page 31, lines 17-19, that the level of AGE-1 expression in the presence of a candidate molecule is compared to the level measured for the same cells in the absence of the candidate molecule. This is the appropriate control for the claimed method, and it is set forth clearly in Appellants' specification.

With respect to the selection of candidate compounds, Appellants direct the Board to page 31, lines 19-21, where Appellants teach that preferred candidate modulators are those that decrease AGE-1 expression, as required by the instant claims. Appellants go on to teach, at page 32, lines 1-7, that such compounds may be purified from a mixture using HPLC or FPLC until a single compound is demonstrated to modulate AGE-1 expression. Appellants further disclose, at page 33, lines 4 and 5, that the usefulness of compounds, found to effectively modulate AGE-1 expression, can be confirmed by testing the compounds in animal models, for example, in nematodes. Finally, Appellants disclose, at page 33, lines 6-9, that selected compounds may be used as therapeutics to decrease the level of native AGE-1 expression and thereby increase the longevity of an animal, for example, a human. Once more, Appellants'specification fully enables that aspect of the claimed invention.

In view of the above teachings in the specification, it is clear that Appellants have provided an enabling description that would instruct the skilled artisan how to measure AGE-1 expression, how to employ the appropriate controls, and how to select compounds that alter AGE-1 expression. In fact, enablement of these components of the claimed methods is not at issue. Rather, the Office merely questions whether a skilled artisan could know whether the effect of a compound on AGE-1 expression is direct. As discussed above, understanding the mechanism by which AGE-1 expression is modulated is not a requirement of § 112, first paragraph, nor is it a requirement generally for patentability of an invention. The enablement rejection in this case has been maintained in error; it should be reversed.

Conclusion

Appellants respectfully request that the rejection of claims 15, 19, and 20 be reversed. A check for $150.00 for the required appeal fee was submitted on November 5, 2002. If there are any additional charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Appendix of Claims on Appeal

15. (Thrice Amended) A method of identifying an AGE-1 modulatory compound that is capable of decreasing the expression of an AGE-1 gene, said method comprising the steps of:

(a) providing a nematode cell expressing its endogenous AGE-1 DNA,

(b) contacting said nematode cell with a candidate compound; and

(c) measuring AGE-1 gene expression in said nematode cell, a decrease in AGE-1 gene expression in said nematode cell following contact with said candidate compound, compared to AGE-1 gene expression in a nematode cell that is not contacted with said candidate compound, identifying said candidate compound as a compound that is capable of decreasing AGE-1 gene expression.

19. (Amended) The method of claim 15 or 16, wherein said method is carried out in a nematode

20. (Amended) The method of claim 15 or 16, wherein said method involves assaying AGE-1 PI 3-kinase activity *in vitro*.